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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/422,528	10/21/1999	WOON-LAM Susan LEUNG	P1190R1	5652

7590 11/21/2005

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EXAMINER
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FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/422,528	Applicant(s) LEUNG ET AL.	
	Examiner Christian L. Fronda	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 October 1999 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/24/2005 has been entered.
2. Claims 1-25 are under consideration in this Office Action.
3. The rejection of claims 1-25 under 35 U.S.C. 102(a) as being anticipated by Leung et al. (Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), BIOT-014. American Chemical Society: Washington, D. C.; reference of record) in view of the Declaration of Woon-Lam S. Leung and James R. Swartz filed 08/24/2005.

### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 1-25 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.  
Applicants' arguments filed 08/24/2005 have been fully considered but they are not persuasive. Applicants' position is that the identity of a particular nucleic acid encoding either the lysozyme or polypeptide and the promoter is not essential to the claimed invention. The Examiner respectfully disagrees for reason of record as supplemented below.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001, which states:  
"Eli Lilly explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of

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compounds is claimed. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1<sup>st</sup> column, line 47 to 2<sup>nd</sup> column, line 2).

The claims are genus claims encompassing a method using a genus of nucleic acids encoding any phage lysozyme of any structure and amino acid sequence, a genus of promoters of any nucleotide sequence and structure, a genus of nucleic acids encoding any signal sequences of any amino acid sequence and structure, a genus of nucleic acids encoding any heterologous polypeptide. A review of the specification including Examples I and II reveals that each genus is essential and critical to the practice of the claimed method.

The scope of each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing nucleotide and/or amino acid sequences. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exists.

While the specification discloses plasmid pIGFLysAra containing a nucleotide sequence encoding IGF-I and lamB signal sequence and a nucleotide sequence encoding T4-lysozyme and ara promoter, the recitation of the names of each genus (e.g., nucleic acid encoding phage lysozyme, promoter, nucleic acid encoding a signal sequence) does not define any structural features commonly possessed by each claimed genus nor define any structural features commonly possessed by each claimed genus. Furthermore, the specification does not describe and define any structural features commonly possessed by each claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and

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(2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of genus of nucleic acids encoding any phage lysozyme of any structure and amino acid sequence, a genus of promoters of any nucleotide sequence and structure, a genus of nucleic acids encoding any signal sequences of any amino acid sequence and structure, a genus of nucleic acids encoding any heterologous polypeptide.

### *Claim Rejections - 35 U.S.C. § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-7, 9-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. (BIO/TECHNOLOGY Vol 12, November 1994; PTO 1449 dated 03/06/2000) in view of Wetzel et al. (EP 0155189; PTO1449 dated 03/06/2000).

Hart et al. teach a process for large scale production of IGF-I from the periplasm of *E.coli* comprising culturing *E.coli* host cell having a plasmid comprising an inducible promoter and nucleic acid encoding a signal sequence for secretion into the periplasm linked to human IGF-I (see entire publication, especially pp. 1113-1115).

Wetzel et al. teach a plasmid vector comprising an inducible promoter and nucleic acid encoding a T4 phage lysozyme (see entire publication, especially pp.3-7 and claims1-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Hart et al. such that the *E.coli* host cell is further transformed with the plasmid vector of Wetzel et al., the host cells are mechanically disrupted to release the IGF-I from the periplasm, and the IGF-I is recovered in the presence of EDTA. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to have

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synthesis of lysozyme which ruptures the polysaccharide membrane of the *E.coli* host cell and simplifies the purification of the human IGF-I. Furthermore, it would have been obvious to one of ordinary skill in the art to construct a vector having the nucleic acid encoding the T4 lysozyme and nucleic acid encoding human IGF-I on the same vector for the purposes of having a only a single vector which simplifies transformation in the *E.coli* host cell.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly *prima facie* obvious.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. in view of Wetzel et al. as applied to the claims above, and further in view of Wick et al. (Infect Immun. 1993 Nov;61(11):4848-56; PTO 892).

Wick et al. teach the nucleic acid encoding the lamB signal sequence for expression in the periplasm of *E.coli* (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the modified method of Hart et al. such that the nucleic acid encoding the lamB signal sequence is used in the plasmid vector having the nucleic acid encoding the human IGF-I. One of ordinary skill in the art at the time the invention was made would have been motivated to do this so that the human IGF-I can be secreted into the periplasm of the *E.coli* host cell. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly *prima facie* obvious.

9. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hart et al. in view of Wetzel et al. as applied to the claims above, and further in view of Balbas et al. (Gene. 1996 Jun 12;172(1):65-9; PTO 892).

Balbas et al. teach the plasmid pBRINT which is an efficient vector for chromosomal integration of cloned DNA into the lacZ gene of *Escherichia coli*, method for integrating cloned DNA into the *E.coli* chromosome using said plasmid pBRINT, and that integration of cloned DNA into the chromosome of the host organism is advantageous with respect to stability or undesired copy number effects (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the modified method of Hart et al. such that the nucleic acid encoding the human IGF-I is cloned into the plasmid pBRINT taught by Balbas et al. which in turn is integrated into the *E.coli* chromosome. One of ordinary skill in the art at the time the invention was made

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would have been motivated to do this to obtain stability of the nucleic acid encoding the human IGF-I and avoidance of undesired plasmid copy number effects as taught by Balbas et al.. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly *prima facie* obvious.

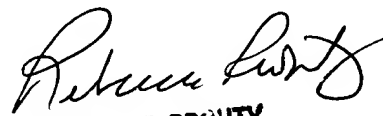
### ***Conclusion***

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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